

AMENDMENTS TO THE SPECIFICATION

Please amend the specification as shown:

Please delete the paragraph on page 14, lines 4-23 and replace it with the following paragraph:

Figure 1 depicts the rifampicin (Rif)^R resistant regions of the RNAP β subunit. The bar on top schematically represents the *E. coli* β subunit primary sequence with amino acid numbering shown directly above. Gray boxes within the schematic indicate evolutionarily conserved regions among all prokaryotic, chloroplast, archaeobacterial, and eukaryotic sequences labeled A-I at the top [Allison *et al.*, *Cell* **42**:599-610 (1985); Sweetser *et al.*, *Proc.Natl.Acad.Sci.USA* **84**:1192-1196 (1987)]. Red markings indicate the four clusters where Rif^R mutations have been identified in *E. coli* [Jin and Gross, *J.Molec.Biol.*, **202**:45-58 (1988); Lisitsyn *et al.*, *Bioorg Khim* **10**:127-128 (1984); Lisitsyn *et al.*, *Molec.Gen.Genet.*, **196**:173-174 (1984); Ovchinnikov *et al.*, *Molec.Gen.Genet.* **190**:344-348 (1983); Severinov *et al.*, *J.Biol.Chem.*, **268**:14820-14825 (1993); Severinov *et al.*, *Molec.Gen.Genet.*, **244**:120-126 (1994)] denoted as the N-terminal cluster (N), and clusters I, II and III (I, II, III). Directly below is a sequence alignment spanning these regions of the *E. coli* (E.c.)(SEQ ID NOS 5-8, respectively, in order of appearance), *T. aquaticus* (T.a.)(SEQ ID NOS 9-12, respectively, in order of appearance), and *M. tuberculosis* (M. t)(SEQ ID NOS 13-16, respectively, in order of appearance) RNAP β subunits. Amino acids that are identical to *E. coli* are shaded dark gray, and those that are homologous (ST, RK, DE, NQ, FYWIV (SEQ ID NO: 29)) are shaded light gray. Mutations that confer Rif^R in *E. coli* and *M. tuberculosis* are indicated directly above (for *E. coli*) or below (for *M. tuberculosis*) as follows: Δ for deletions, Ω for insertions, and colored dots for amino acid substitutions (substitutions at each position are indicated in single-amino acid code in columns above or below the positions). The yeast, human and Drosophila fragments are shown in SEQ ID NOS 17-28, respectively, in order of appearance.

Please delete the paragraph on page 18, lines 1-27 and replace it with the following paragraph:

Figures 6a and 6b (SEQ ID NO: 30) show the mechanism of RNAP inhibition by rifampicin. The RNAP active site Mg^{2+} (magenta sphere) and the 9-basepair RNA/DNA hybrid (from +1 to -8) from a model of the ternary elongation complex [Korzheva *et al.*, *Science* **289**:619-625 (2000)] are shown in Figure 6a. The RNAP itself and the rest of the nucleic acids are omitted for clarity. The incoming nucleotide substrate at the +1 position is colored green, the -1 and -2 positions, which can be accommodated in the presence of rifampicin, are colored yellow. The RNA further upstream (-3 to -8), which cannot be accommodated in the presence of rifampicin is colored pink. The template strand of the DNA is colored grey. Also shown is a CPK representation of rifampicin as it would be positioned in its binding site on the β subunit (carbon atoms, orange; oxygen, red; nitrogen, blue). The rifampicin is partially transparent, illustrating the RNA nucleotides at -3 to -5 that sterically clash. This depiction was generated using GRASP [Nicholls *et al.*, *Proteins Structure, Function and Genetics* **11**:281-296 (1991)]. The structure of the minimal scaffold systems with RNA lengths from 3-7 nucleotides (labeled above the RNA chain) are shown in Figure 6b [Korzheva *et al.*, *Science* **289**:619-625 (2000)]. The results are presented below as autoradiographs of the radioactive RNAs produced by *E. coli* (lanes 1-15) or *Taq* (lanes 16-30) core RNAPs transcribing the minimal scaffolds with the indicated lengths of RNA ('X =') and analyzed on a 23% polyacrylamide gel. Lanes 1-10 and 16-25 demonstrate the effect of rifampicin inhibition on transcription when it was bound by RNAP either before (lanes 1-5 and 16-20) or after (lanes 6-10 and lanes 21-25) addition of the scaffold. Lanes 11-15 and 26-30 show elongation of the same scaffolds in the absence of rifampicin. The RNA with the critical length of 3 nucleotides which cannot be elongated by *E. coli* RNAP in the presence of rifampicin regardless of the order of rifampicin and scaffold addition (lanes 1,6) is colored red. The RNAs of 4-7 nucleotides (colored green) were extended by *E. coli* RNAP when added before rifampicin (lanes 6-10).